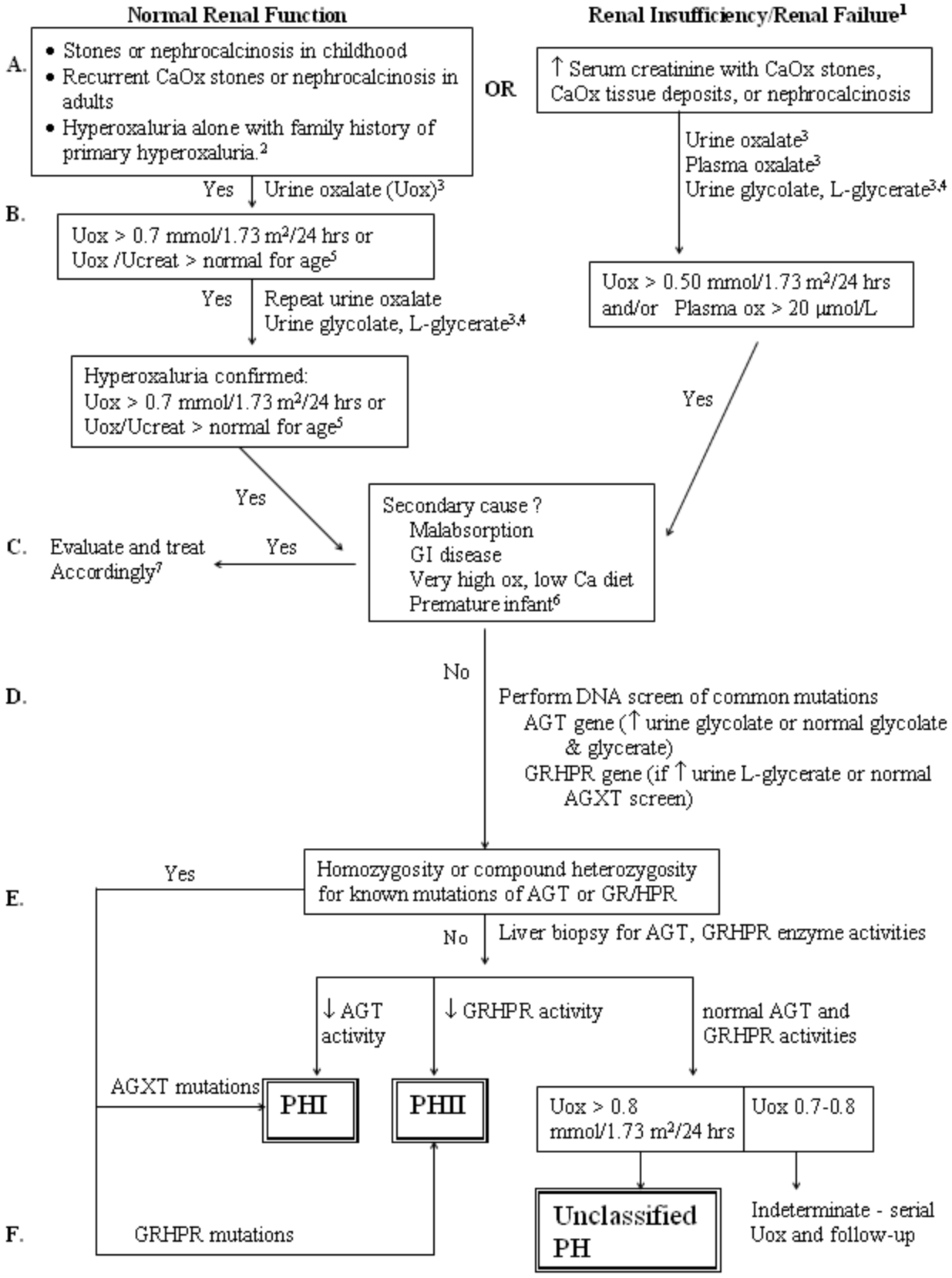

Figure 1. Diagnostic algorithm for individuals with suspected PH1. Algorithm and annotations reprinted with permission from S Karger AG, publisher [Milliner 2005].

Figure 1 Annotations:

1. Renal insufficiency or renal failure is defined as a glomerular filtration rate (GFR) less than 50 mL/min/1.73 m^2, or serum creatinine that is greater than or equal to 2 times normal for age.
2. The guideline does not address prenatal diagnosis [Danpure & Rumsby 1996, Rumsby 1998].
3. Urine and plasma oxalate and urine glycolate measurements for diagnostic testing should be obtained while the patient is receiving no pyridoxine or vitamin supplements.
4. Increased urine glycolate, in the presence of hyperoxaluria, is suggestive of P, type 1. Increased urine L-glycerate in a hyperoxaluric patient suggests PH type 2.
5. Urine oxalate/creatinine ratios in healthy children vary continuously by age. Normal values tables should be consulted in interpretation of any random urine oxalate/creatinine. To convert mg/mg to mmol/mmol, multiply by 1.28.

Random ("spot") urine oxalate/creatinine by age [Barratt et al 1991, von Schnakenburg et al 1994, Gibbs & Watts 1969, Morgenstern et al 1993, Kasidas & Rose 1987]:

Age of affected individual	**Upper limit of normal (mmol/mmol)**
Infants (<6 months)	0.37
>6 months - 2 years	0.26
>2 years	0.14
6 -12 years	0.08

Little data are available to guide interpretation of random urine oxalate/creatinine in adolescents and adults. Upper limit of normal ratios declining to 0.04 by age 18-20 years and then remaining stable through adult ages are suggested by available literature [Milliner et al 1994, Gibbs & Watts 1969]. In patients of all ages, confirmation of hyperoxaluria by a 24 hour urine collection with normalization of the oxalate excretion rate to 1.73 m^2 body surface area, is strongly recommended. From 2 years of age through adulthood, normal urine oxalate is constant at <0.45 mmol/1.73 m2/24 hours [Gibbs & Watts 1969].

6. Urine oxalate/creatinine ratios are higher in very premature infants than in term infants, especially when they are receiving parenteral nutrition containing amino acids. The ratio falls when premature infants are receiving only glucose and electrolyte solutions [Campfield & Braden 1989].
7. When very high oxalate or low dietary calcium is suspected as the cause of the hyperoxaluria, the diet should be corrected and the urine oxalate remeasured for verification.

Note: In a recent survey of American nephrologists, only 40% of individuals treated for PH1 had a diagnostic liver biopsy. Diagnosis was usually based on history and urinary oxalate excretion. Measurement of glycolate and L-glyceric acid excretion, required to distinguish PH1 from PH2, was rarely performed [Hoppe & Langman 2003]. On average, five years elapsed between the initial symptoms and the achievement of the correct diagnosis [Cochat et al 1995, Lieske et al 2005].